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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/707,320	11/07/2000	Susan B. Sobolov-Jaynes	PC10408A	9424

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EXAMINER	
HENLEY III, RAYMOND J	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/707,320	SOBOLOV-JAYNES, SUSAN B.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1-16 ARE PRESENTED FOR EXAMINATION

Applicant's "Response to Non-Compliant Appeal Brief (37 C.F.R. 41.37)" and declarations of Stafford McLean (37 C.F.R. § 1.132) filed December 12, 2005 have been received and entered into the application.

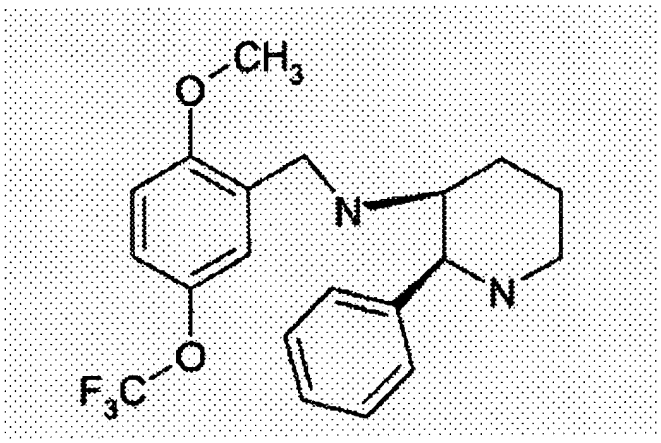
In view of the newly filed status of the above declarations and the new reference applied by the Examiner, below, the finality of the Office action dated September 24, 2002 is *withdrawn* so that the Examiner may properly consider the declarations and apply the newly cited reference. The Examiner regrets the delay in citing such reference, however the application has just recently come before the Examiner for action.

It should be noted that the present Examiner is not the same Examiner who had examined the application at the time of the issuance of the Advisory Action dated May 7, 2003. The present Examiner, however, is of the same opinion as the previous Examiner that a showing of unexpected would overcome the present and previous conclusions of obviousness. It should be, of course, be recognized that any such showing must be commensurate in scope with the claimed subject matter to merit withdrawal of the rejection, (see MPEP § 2144.08(II)(B)).

Election/Restriction

The claims remain subject to the election of species requirement set forth in the Office action dated October 16, 2001 and maintained in the Office actions thereafter.

The elected species, (such election being traversed in Applicant's response dated January 9, 2002), remain as (a) a compound of the formula:



which has the chemical name (2S,3S)-3-(2-methoxy-5-trifluromethoxybenzyl)-amino-2-phenylpiperdine, (the chemical as depicted on the last page of Applicant's paper filed January 9, 2002, referred to in the previous Office actions as "CP 122721" and disclosed in the present specification at page 29, line 6. The elected compound (b), which corresponds to the claimed "compound that exhibits activity, respectively, as an anxiolytic agent or an antidepressant or a pharmaceutically acceptable salt thereof", (see, e.g., present claim 1), and is sertraline, (see the last page of Applicant's paper filed January 9, 2002 and the present specification at, for example, page 4, line 32).

Conflicting Claims

Claims 1-16 of this application conflict with claims 1-16 of Application No. 10/856,029. 37 CFR 1.78(b) provides that when two or more applications filed by the same Applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one

application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Claim Rejection - 35 USC § 103

Claims 1-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe, III et al. (U.S. Patent No. 5,773,450, "Lowe"), in view of The Merck Index, ("Merck"), each already of record, for the reasons of record as maintained in the Advisory Action dated May 7, 2003, and further in view of Harrison's Principles of Internal Medicine, (newly cited by the Examiner, "Harrison's").

In the previous Office actions, the motivation to combine the teachings of Lowe and Merck was based solely on the court's decision of See In re Kerkhoven 205 U.S.P.Q. 1069 (CCPA 1980) and the cases cited therein. That is, because both species were known to be effective for the treatment of depression, it would have been obvious to one of ordinary skill in the art to combine such antidepressants because it has been held that it is considered prima facie obvious to have combined two or more ingredients each of which was known to be useful for the same purpose in order to form a third composition that is useful for the very same purpose. The idea for combining them flows logically from their have been used separately. Further, the skilled artisan would have been motivated to combine such ingredients in order to achieve at least additive results and to provide the individual being treated with the most convenient, effective therapy possible.

Here, the Examiner wishes to further the position that one of ordinary skill in the art would have been motivated to combine two known antidepressants. In particular, Harrison's

teaches that "[p]atients who have complicated psychiatric histories or fail to respond to the initial [antidepressant] medication trial should be referred for psychiatric consultation. This may lead to *medication combination (augmentations)* or other sophisticated treatment such as electroconvulsive therapy (ECT). Insofar as the patients of Harrison's are not outside of the scope of the present claims, it is further believed that one of ordinary skill in the art would have been motivated to combine the antidepressants of the prior art in order to treat just the patient population that is taught in Harrison's.

Accordingly, the claims are deemed properly rejected.

Consideration of Applicant's Remarks/Exhibits A &B

Applicant's remarks in the above referenced response and the declarations of Stafford McLean, ("the Mclean declarations") have been considered in this matter, but fail to persuade the Examiner of error in his determination of obviousness, which determination has been addressed anew in light of such remarks and the Mclean Declarations.

Applicants at pages 5 and 6 of their response have taken the position that the McLean declarations are evidence of unexpected results an thus, "there is no valid reason why the present method invention for the treatment of depression involving a CNS-penetrant NK-1 receptor antagonist in combination with an antidepressant or an anxiolytic should not be fully allowable.

In response thereto, the Examiner first notes the McLean declaration in which a report entitled "Cognos Plus Study #11, The Emerging Antidepressant Market Through 2014-Focus on Emerging Therapies and New Indications", (the Cognos Study"), is relied upon to apparently lend credence to what appears to be the declarant's optimism for the combination of an NK-1 antagonist and an antidepressant in the treatment of depression.

The Examiner considers this to be an opinion declaration. While the report relied on does touch upon the expected market share and the profits which may be enjoyed, it has not been offered as a showing of commercial success. In addressing this declaration, the Examiner is guided by the MPEP § 716.01(c)(III) which is entitled "Opinion Evidence". In particular, it is set forth therein that "While an opinion as to a legal conclusion is not entitled to any weight, the underlying basis for the opinion may be persuasive. *In re Chilowsky*, 306 F.2d 908, 134 USPQ 515 (CCPA 1962)". Also, it is stated "In assessing the probative value of an expert opinion, the examiner must consider the nature of the matter sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985), cert. denied, 475 U.S. 1017 (1986)." Here, the Examiner will consider the underlying basis for declarant's opinion, i.e., the Cognos study. Further, in the above section of the MPEP it is set forth ".

In the declaration addressing the Cognos study, i.e., referred to as "Exhibit B", (see page 5 of the appeal brief at page 5, third paragraph), declarant has set forth substantially what is set forth in the Cognos Study at page 6, second paragraph. This section of the study sets forth that the combination of an NK1 antagonist and a selective serotonin reuptake inhibitor (SSRI), (the elected species (b), i.e., sertraline, is a selective serotonin reuptake inhibitor, see Merck at line 5 of the Sertraline monograph), "is of significant interest to thought leaders because recent development activity surrounding [the NK-1 antagonist] shows that this class of agents, once thought to lack potential in the antidepressant market, does indeed possess competitive potential as antidepressants", (Exhibit B at page 1 and the Cognos Study at page 6, second paragraph).

This fails to persuade the Examiner that the instant conclusion of obviousness is without merit because such statement is apparently made without benefit of the teachings of Lowe et al., relied on herein to show that the elected NK-1 antagonist possesses antidepressant activity.

The Cognos study further states that "Physician confidence in the efficacy of [a combination of a NK-1 antagonist and an SSRI antidepressant], and the anticipated favorable tolerability profile of the addition of the substance P antagonists, [i.e., the NK-1 antagonists], indicates that the NK1/SSRI combination pill will offer a clinically differentiated option in the crowded antidepressant market when it launches in 2011, as a result garnering peak-year sales within the $1-2 billon range", (the Cognos study at page 6 and Exhibit B at page 2).

This fails to persuade the Examiner of error in his conclusion of obviousness because the statement appears to go to the novelty of an NK1/SSRI combination and the novelty of such a combination is not an issue in the present rejection, i.e., in making the rejection under 35 U.S.C. § 103, the Examiner implicitly admits that the combination of the elected species is novel. Further, such statement appears to go to the *expected* commercial success of a combination product. When commercial success is relied on as a secondary consideration, at the very least, such success must be realized and not merely anticipated. This position is implicit throughout MPEP § 716.03, where commercial success is referred to as having already occurred, e.g., "An applicant who is asserting commercial success to support its contention of nonobviousness bears the burden of proof of establishing a nexus between the claimed invention and evidence of commercial success., (*Id.* at section I). Further, even if commercial success was established on the record by the evidence proffered by Applicants, such success would only be associated with one particular combination of ingredients, and such is not commensurate in scope with either the

claimed subject matter or the species elected for examination purposes, (see *infra* regarding the necessity of evidence being commensurate in scope with the claimed subject matter).

Accordingly, Applicant's Exhibit B, and the documents associated therewith, fail to persuade the Examiner of error in his determination of obviousness.

Respecting the Mclean declaration referred to by Applicants as Exhibit A, and the data shown in the Exhibit, as well as the graphical representation of such data, the Examiner *will agree* with Applicant and the declarant that such evidence establishes results that would not have been expected by one of ordinary skill in the art. The evidence shows that in a animal model recognized in the art to be predictive of anxiolytic activity, a combination of "CJ-011974-01" (declaration at page 3, following the heading "Drugs/doses" above the chart), which has not been chemically identified in either of the appeal brief or Exhibit A, and Sertraline produced an unexpected degree of anxiolytic activity, i.e., the combination showed more than additive effects, (a.k.a. synergy). Such evidence, however, is not commensurate in scope with the claimed subject matter, and thus cannot be afforded the significance urged.

With regard to the requirement that the evidence of non-obviousness be commensurate in scope with the claimed subject matter, the Examiner is guided by MPEP § 716.02(d). The first reason why the evidence is not commensurate in scope with the claimed subject matter is that such evidence is directed to anxiolytic activity while the conclusion of obviousness rests upon that portion of the claims which is directed to the antidepressant activity. It has not been established on the record that anxiolytic activity may be extrapolated to, or predictive of, antidepressant activity.

Further, even if the compound "CJ-011974-01" was chemically identified and the results were directed to antidepressant activity, the evidence involves only a single combination of compounds and it has not been established on the record that such a combination would allow the artisan to reasonably extend the probative value thereof to the entirety of combinations encompassed by the present claims, much less that it is even the combination of species elected by Applicant for examination. In this regard, it is set forth in the MPEP § 716.02(d)(I) that "Nonobviousness of a Genus or Claimed Range May be Supported by Data Showing Unexpected Results of a Species or Narrower Range Under Certain Circumstances", (the heading), and that "The nonobviousness of a broader claimed range can be supported by evidence based on unexpected results from testing a narrower range if one of ordinary skill in the art would be able to determine a trend in the exemplified data which would allow the artisan to reasonably extend the probative value thereof. *In re Kollman*, 595 F.2d 48, 201 USPQ 193 (CCPA 1979).", (directly under the heading). As stated above, the Examiner is unaware of any statement made by Applicant or the declarant that would establish that the data shown would allow the artisan to extend the probative value thereof to the entire population of combinations encompassed by the present claims.

The MPEP further states (*Id.*), "*In re Lindner*, 457 F.2d 506, 509, 173 USPQ 356, 359 (CCPA 1972) (Evidence of nonobviousness consisted of comparing a single composition within the broad scope of the claims with the prior art. The court did not find the evidence sufficient to rebut the prima facie case of obviousness because there was 'no adequate basis for reasonably concluding that the great number and variety of compositions included in the claims would behave in the same manner as the tested composition.').". This is exactly the situation at

hand (if antidepressant activity was shown and the identity of the compound "CJ-011974-01" were disclosed). Accordingly, the Examiner is compelled to not give Exhibit A the significance urged by Applicant and therefore, maintain the rejection as being proper.

Double Patenting

Statutory-Provisional

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-16 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-16 of copending Application No. 10/856,029. This rejection is proper because the co-pending claims and the present claims are (i) pending and (ii) directed to exactly the same subject matter. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Obviousness-Type, Provisional

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 10/388,383, (the claims are subject to a restriction/election requirement, but nevertheless are pending). Although the conflicting claims are not identical, they are not patentably distinct from each other because a one-way test of obviousness allows for the conclusion that the subject matter of the present set of claims and the subject matter of co-pending set of claims would have been obvious. The co-pending claims are directed to the same therapeutic objective as in the present claims and require the presence of a PDE IV inhibitor and such is not required in the present claims. However, the present claims recite "comprising" and thus do not patentably exclude other components, such as the PDE IV inhibitors of the co-pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

March 18, 2006